

Tidlig opsporing af alkoholrelateret leversygdom

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Interessekonflikter

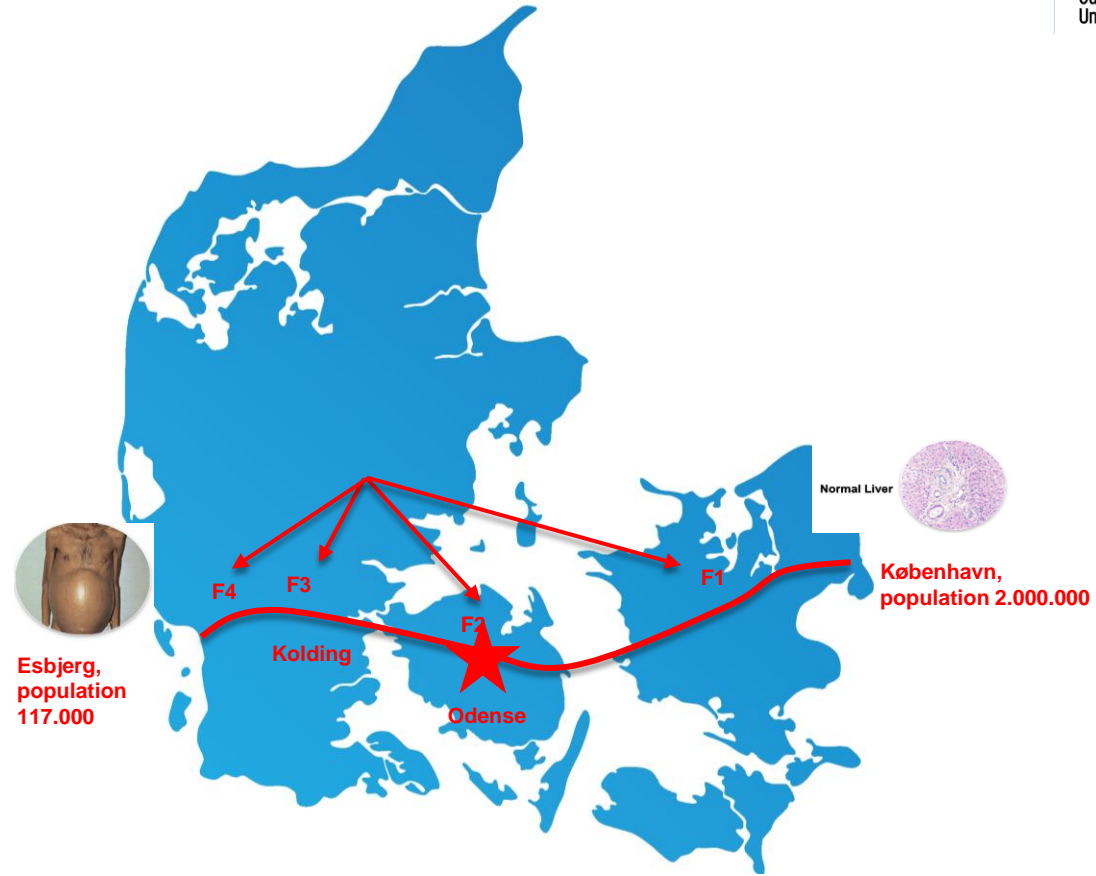
Honorarer fra EchoSens, Siemens Healthcare, Norgine, GE Healthcare

European grants:

- GALAXY (H2020 number 668031)
- LiverScreen (H2020 number 847989)
- MicrobPredict (H2020 number 825694)
- MicrobLiver (NNF 15OC0016692)
- DECIDE (NNF 20OC0059393)

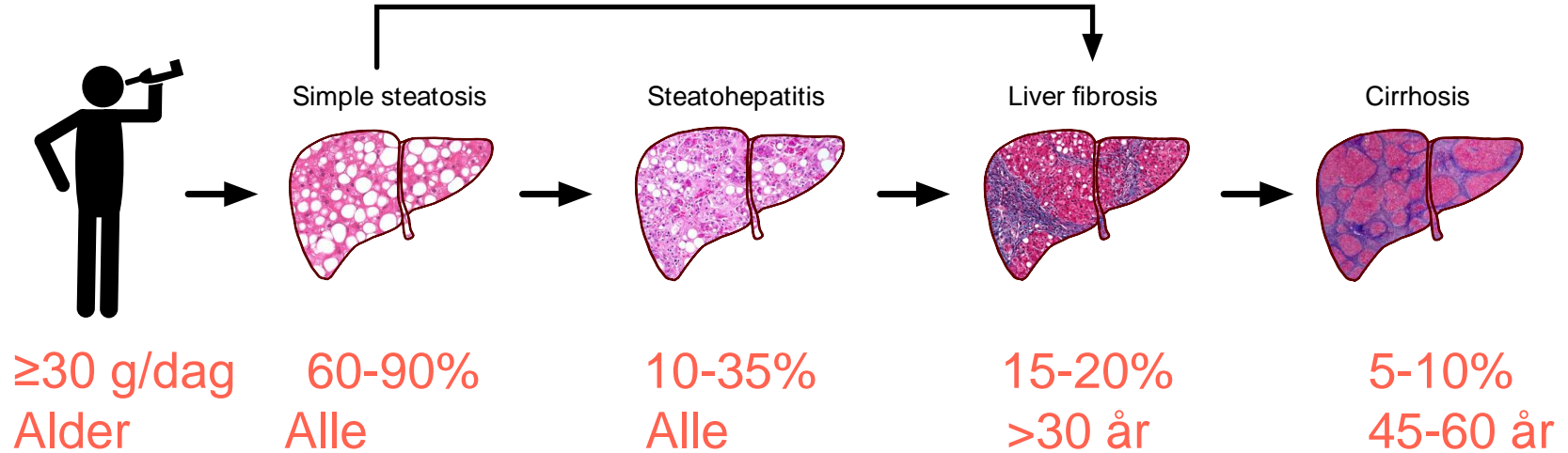


Co-funded by the Horizon 2020 programme
of the European Union



- Kører bilen mod Esbjerg?
- Hvis bilen kører mod Esbjerg, hvor befinder den sig så lige nu?
- Er bilen en Ferrari eller en Peugeot Berlingo, og kører den på 100 eller 92 oktan?
- Hvordan får jeg bilen til at vende om og køre tilbage mod København?

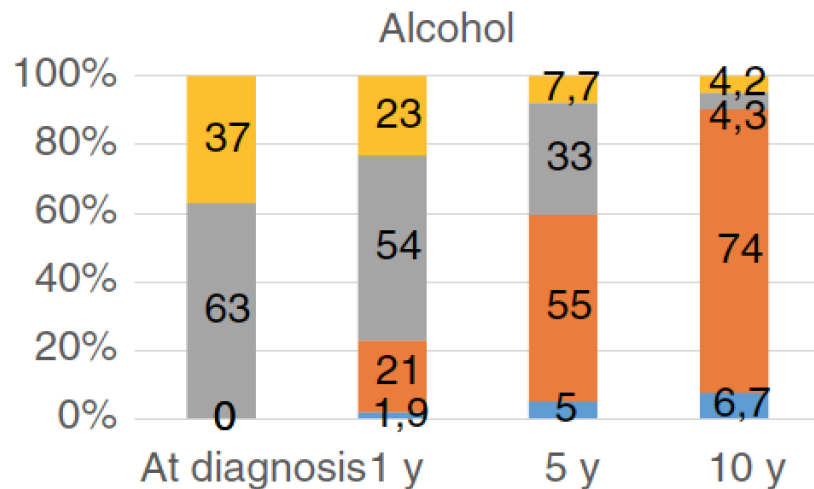
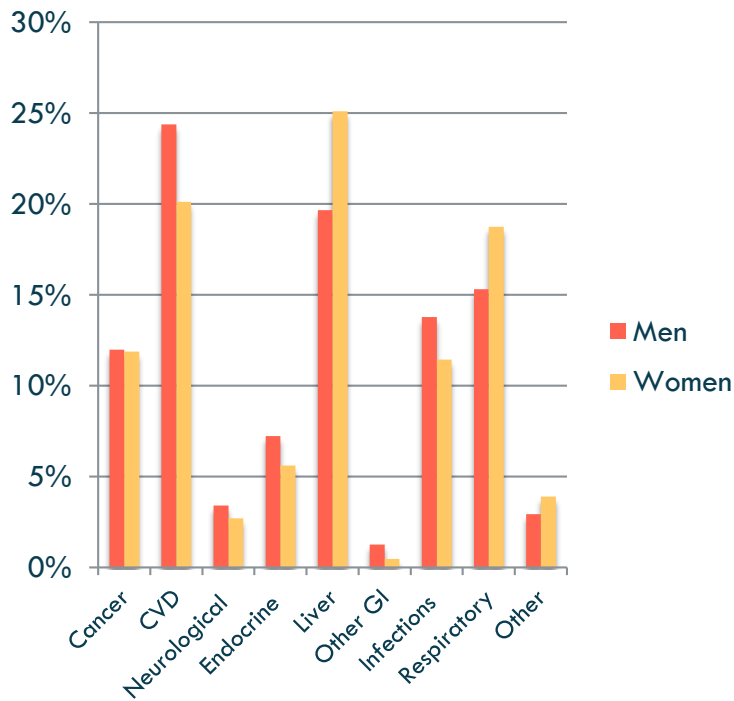
'Naturhistorien' for alkoholrelateret leversygdom



Udfordringen:



Høj dødelighed
Høj sygelighed



Holst, Addiction 2017
Nilsson, APT 2019

Udfordringen:

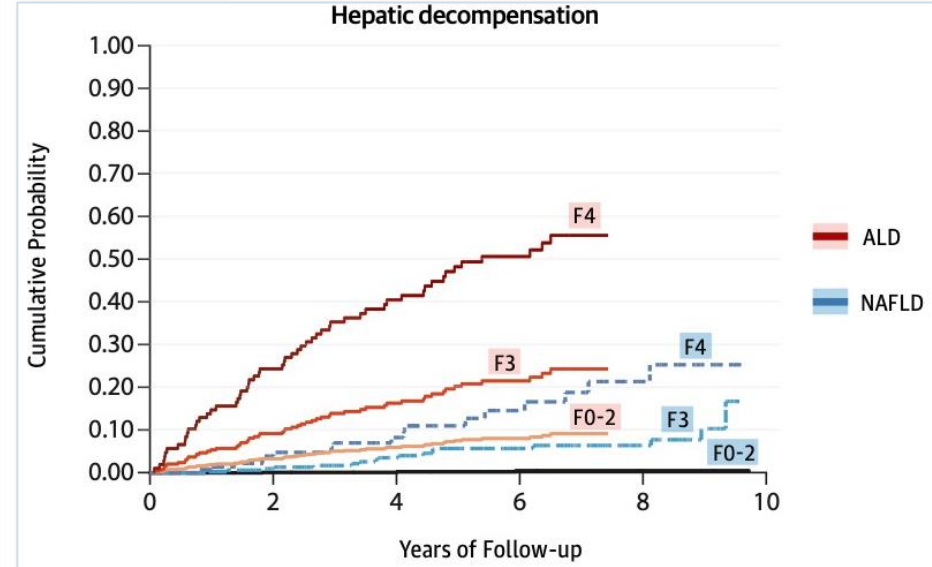
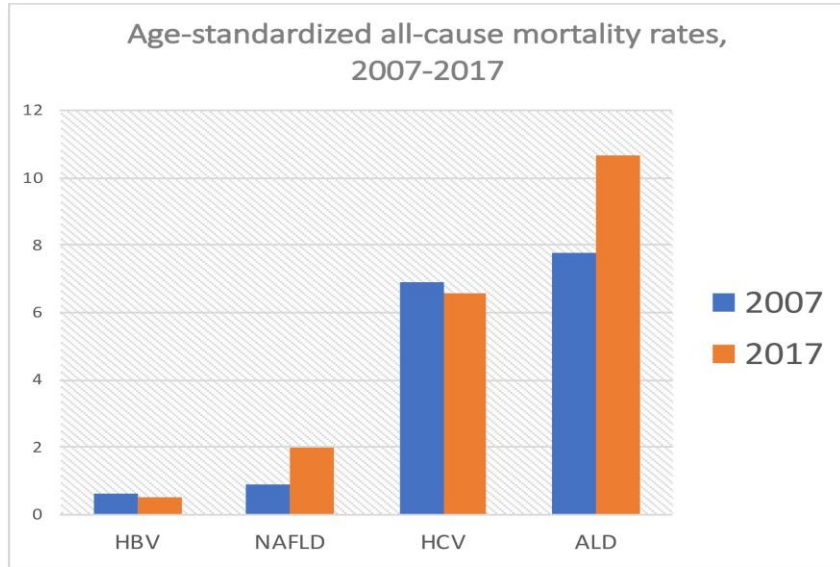


Høj dødelighed
Høj sygelighed

Table 2 Outcome events during follow-up in patients with ALD and matched reference individuals

Characteristic	Overall	Normal liver	Steatosis	Fibrosis	Cirrhosis
ALD population					
N	3453	91	504	482	1780
Inpatient or outpatient visits related to AUD during follow-up, n (%)	1213 (35.1)	29 (31.9)	225 (44.6)	173 (35.9)	609 (34.2)
Deaths or liver transplantation					
Within 1 year after index date	436 (12.6%)	12 (13.2%)	26 (5.2%)	41 (8.5%)	263 (14.8%)
Within 5 years after index date	1413 (40.9%)	25 (27.5%)	137 (27.2%)	165 (34.2%)	831 (46.7%)
Within 10 years after index date	1979 (57.3%)	35 (38.5%)	211 (41.9%)	245 (50.8%)	1 136 (63.8%)
All follow-up time	2557 (74.1%)	57 (62.6%)	314 (62.3%)	316 (65.6%)	1427 (80.2%)
Incidence rate by 1000 PY	90.9 (87.3–94.4)	56.7 (42.0–71.4)	53.5 (47.6–59.5)	80.0 (71.2–88.8)	116.2 (110.2–

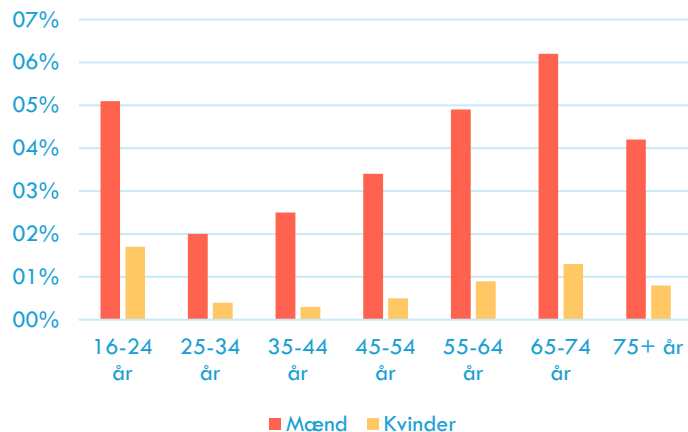
Sammenlignet med andre leversygdomme?



Hvordan opsporer vi leversygdom blandt personer med et højt forbrug af alkohol?

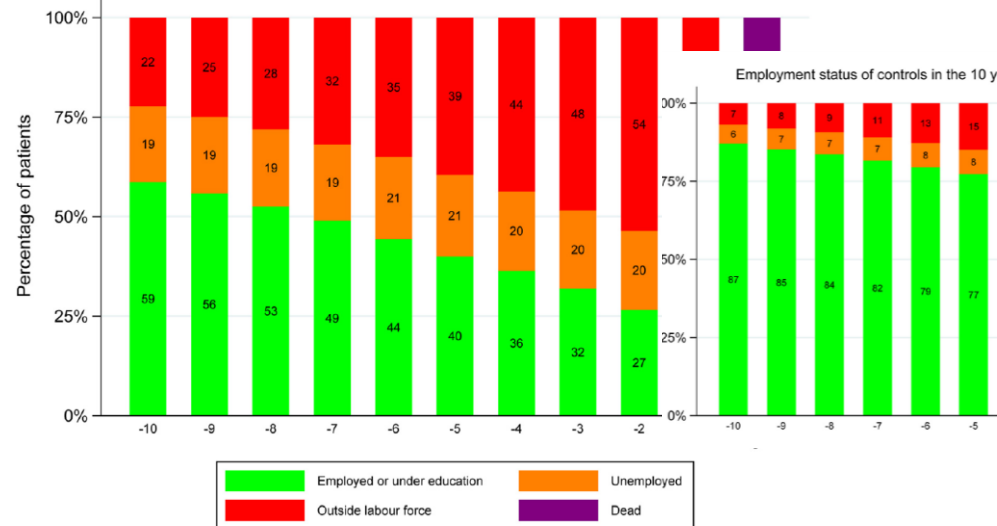
Find de rette mennesker

Sundhedsprofilen 2021: ≥ 30 genst/uge



4.0% mænd & 0.8% kvinder \approx
74.707 mænd og 14.749 kvinder < 70 år
 \approx **90.000 danskere**

Employment status of ALD patients in the 10 years before diagnosis, n = 17,142



Jepsen Lancet Regional Health Europe 2021

- Alle danske alkohol-cirrosepatiser 2009-18
- 86% lav-mellemlav uddannelsesniveau
- ALD incidens: Fra 181 til 910 per mill. PY fra højeste til laveste uddannelsesniveau.

Find de rette mennesker

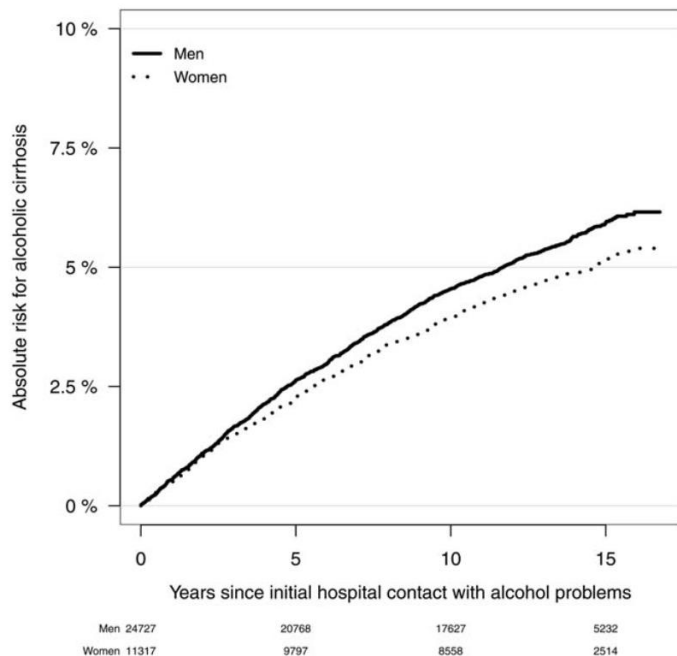
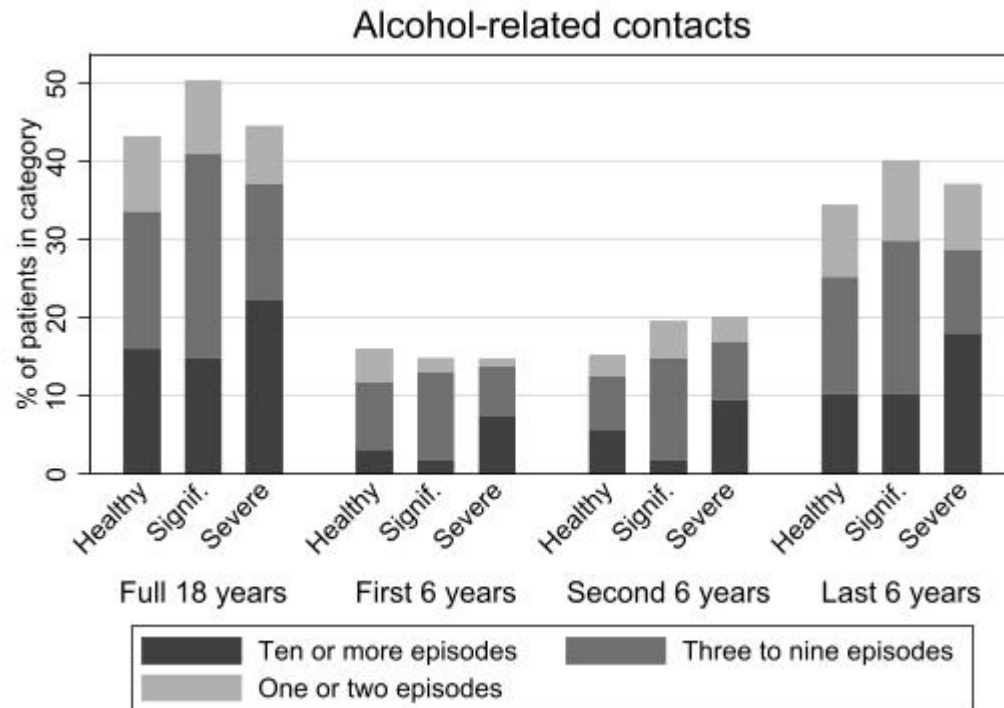


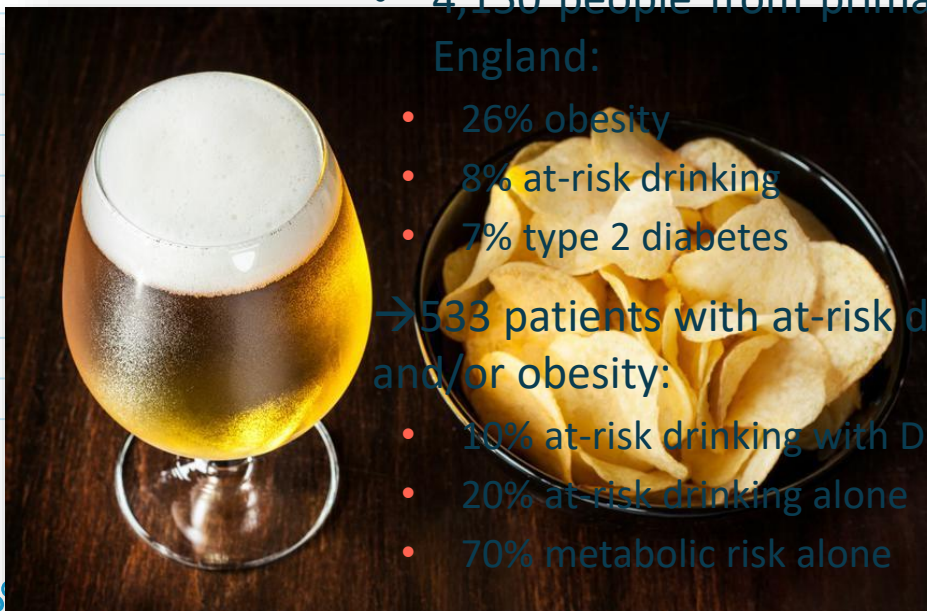
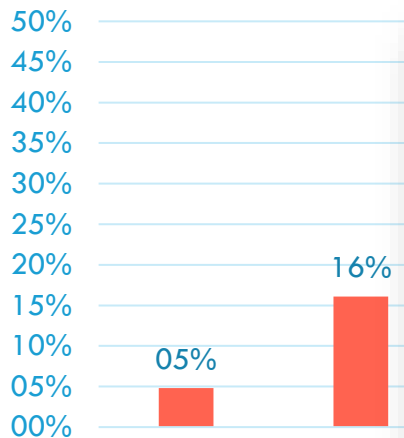
FIG. 1. Absolute risk for alcoholic liver cirrhosis according to years since initial hospital contact with alcohol problems of men and women who had such a hospital contact 1998-2002, n = 36,044.



Askgaard, Hepatology 2017;
Rasmussen, in preparation

En risikabel cocktail: Alkohol & overvægt/DM2

TE \geq 8kPa



- 4,150 people from primary care practices in England:

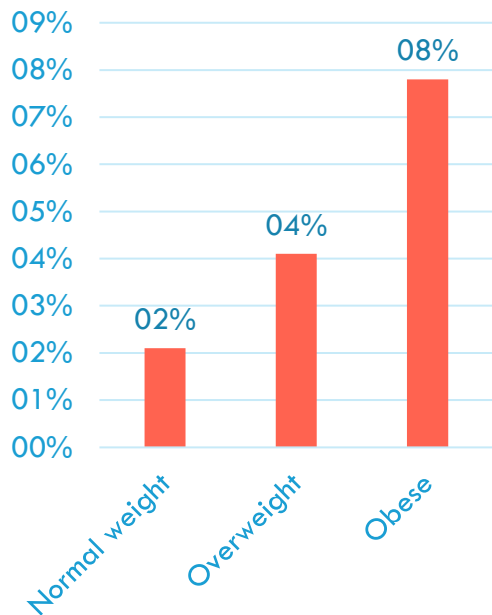
- 26% obesity
- 8% at-risk drinking
- 7% type 2 diabetes

→ 533 patients with at-risk drinking and/or DM2 and/or obesity:

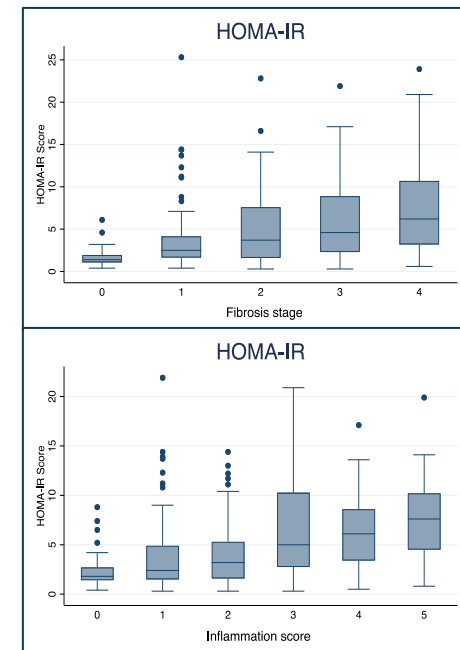
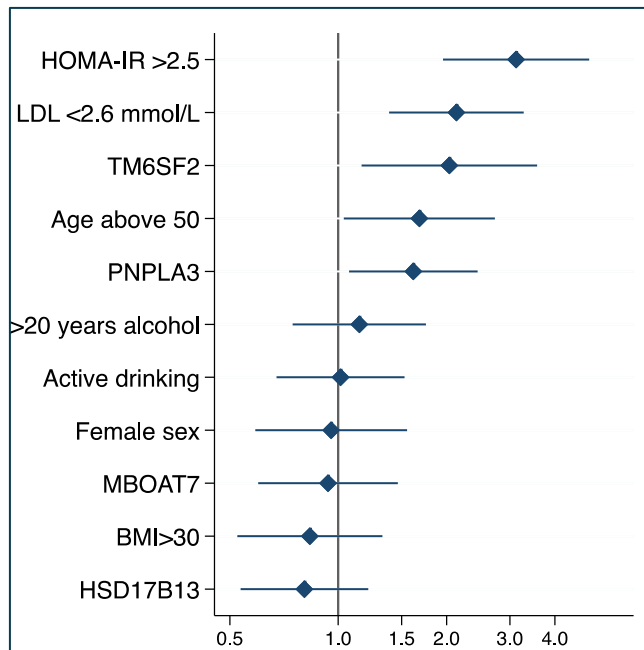
- 10% at-risk drinking with DM2 and/or obesity
- 20% at-risk drinking alone
- 70% metabolic risk alone

En risikabel cocktail: Alkohol, overvægt/DM2, genetik

Deaths with liver disease



Excess drinkers



Hart, BMJ 2010

Israelsen Clin Gas Hep 2021

Brug nøjagtige diagnostiske tests

SDU 

OUH
Odense
University Hospital



- Er de praktiserende læger begrænset af de test, som de har til rådighed?
- Hvordan sikrer man at de rette mennesker henvises til ambulante leverklinikker samtidig med at undgå overdiagnostik og for mange hospitalshenvisninger?

Almen praksis

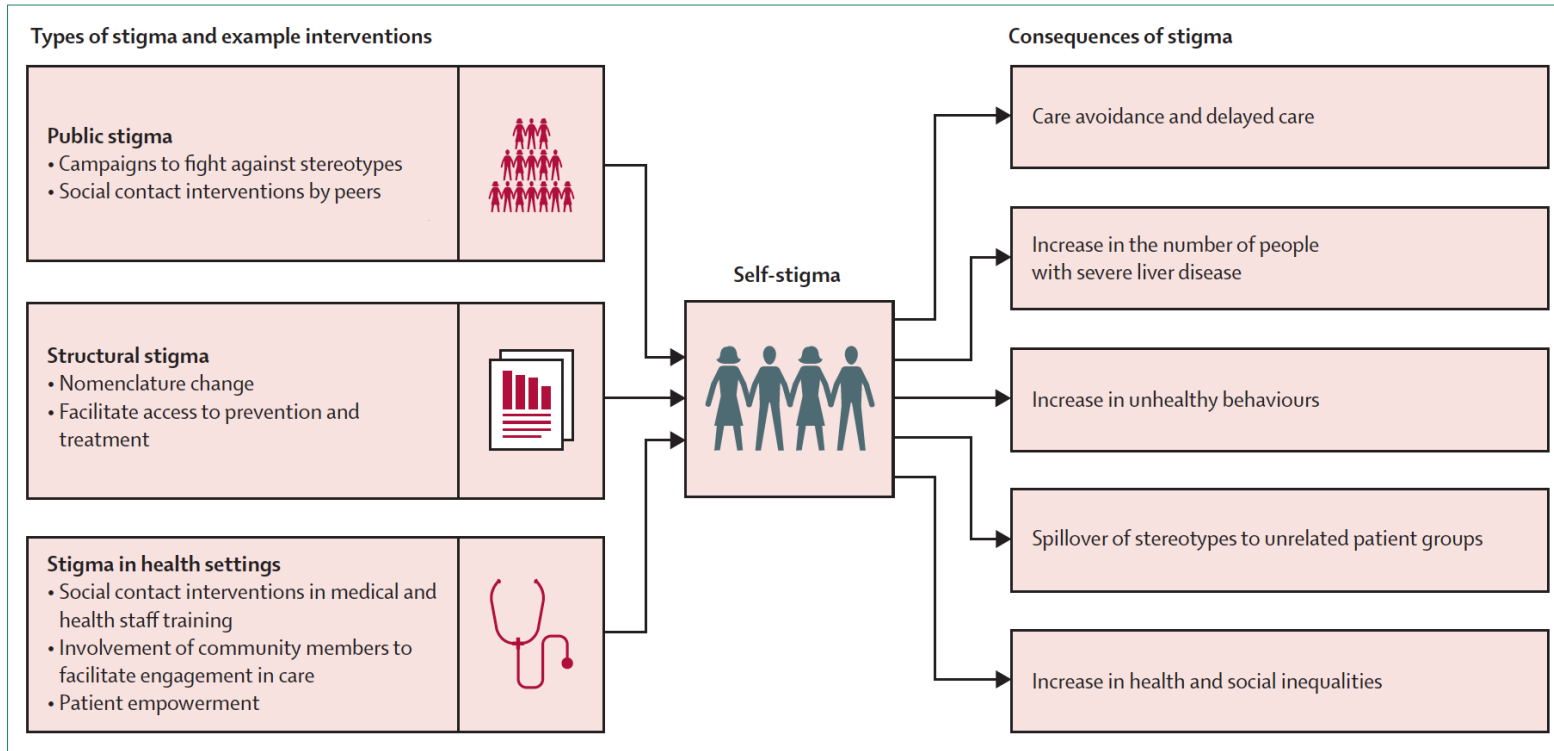
- 24 almen praksis besøg for mænd, relateret til alkohol
- 5 for kvinder
- Alle som døde af alkoholrelateret cirrose havde *mindst* en indikator for overforbrug
- 21% var aldrig blevet rådet til at skære ned på alkoholforbruget

Table 2

Treatment options among 65 individuals who died from alcohol-related causes in 2003, by sex.

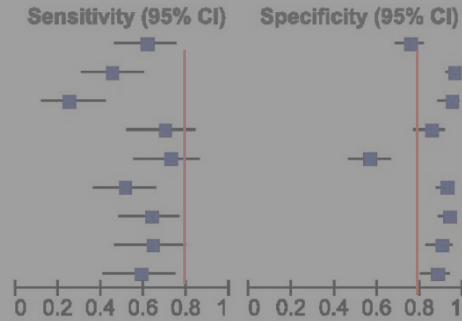
Treatment modality	Male n (%)	Female n (%)	All n (%; 95% CI)
Advice to abstain	41 (85%)	10 (59%)	51 (79%, 67–87%)
Drink diary			
Yes, complied	1 (2%)	0	1 (2%, 3–8%)
Yes, did not comply	1 (2%)	0	1 (2%, 3–8%)
No	46 (96%)	17 (100%)	63 (97%, 90–99%)
Brief intervention			
Yes, complied	3 (6%)	1 (6%)	4 (6%, 2–15%)
Yes, did not comply	10 (21%)	1 (6%)	11 (17%, 10–28%)
No	35 (73%)	15 (88%)	50 (77%, 65–86%)
Psychological intervention			
Yes, complied	8 (17%)	2 (12%)	10 (15%, 9–26%)
Yes, did not comply	11 (23%)	1 (6%)	12 (19%, 11–30%)
No	29 (60%)	14 (82%)	43 (66%, 54–77%)
Prescribed vitamin B	40 (83%)	10 (59%)	50 (77%, 65–86%)
Prescribed parenteral vitamin B (Pabrinex)	19 (40%)	6 (35%)	25 (38%, 28–51%)
Prescribed thiamine	37 (77%)	9 (53%)	46 (71%, 59–80%)
Prescribed disulfiram ^a	2 (4%)	0 (0%)	2 (3%, 8–11%)
Prescribed acamprosate^b	3 (6%)	1 (6%)	4 (6%, 2–15%)

Almen praksis



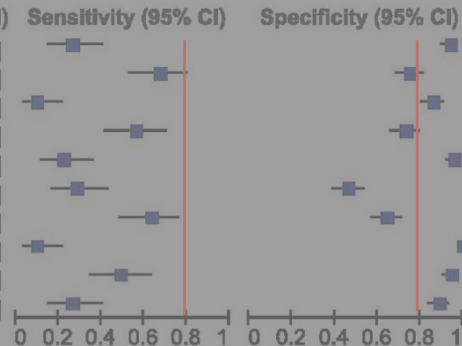
Doctors

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Family doctor 1	30	44	19	132	0.61 [0.46, 0.75]	0.75 [0.68, 0.81]
Family doctor 2	22	8	27	168	0.45 [0.31, 0.60]	0.95 [0.91, 0.98]
Family doctor 3	9	6	27	99	0.25 [0.12, 0.42]	0.94 [0.88, 0.98]
Family doctor 4	25	16	11	89	0.69 [0.52, 0.84]	0.85 [0.76, 0.91]
Family doctor 5	26	46	10	59	0.72 [0.55, 0.86]	0.56 [0.46, 0.66]
Hepatologist 1	25	14	24	162	0.51 [0.36, 0.66]	0.92 [0.87, 0.96]
Hepatologist 2	31	12	18	164	0.63 [0.48, 0.77]	0.93 [0.88, 0.96]
Hepatologist 3	23	11	13	94	0.64 [0.46, 0.79]	0.90 [0.82, 0.95]
Hepatologist 4	21	13	15	92	0.58 [0.41, 0.74]	0.88 [0.80, 0.93]



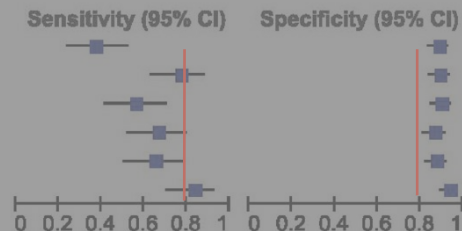
Liver blood tests

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Albumin	13	11	36	165	0.27 [0.15, 0.41]	0.94 [0.89, 0.97]
Alkaline phosphatase	33	44	16	132	0.67 [0.52, 0.80]	0.75 [0.68, 0.81]
ALT	5	25	44	151	0.10 [0.03, 0.22]	0.86 [0.80, 0.91]
AST	27	47	21	127	0.56 [0.41, 0.71]	0.73 [0.66, 0.79]
Bilirubin	11	8	38	168	0.22 [0.12, 0.37]	0.95 [0.91, 0.98]
Cholesterol	14	94	35	81	0.29 [0.17, 0.43]	0.46 [0.39, 0.54]
GGT	31	63	18	113	0.63 [0.48, 0.77]	0.64 [0.57, 0.71]
INR	5	1	44	175	0.10 [0.03, 0.22]	0.99 [0.97, 1.00]
Platelet count	24	10	25	166	0.49 [0.34, 0.64]	0.94 [0.90, 0.97]
Sodium	13	20	36	156	0.27 [0.15, 0.41]	0.89 [0.83, 0.93]



Indirect and direct fibrosis tests

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
APRI	18	20	30	154	0.38 [0.24, 0.53]	0.89 [0.83, 0.93]
ELF	37	19	11	154	0.77 [0.63, 0.88]	0.89 [0.83, 0.93]
FIB-4	27	18	21	156	0.56 [0.41, 0.71]	0.90 [0.84, 0.94]
FibroTest	32	23	16	147	0.67 [0.52, 0.80]	0.86 [0.80, 0.91]
Forns index	32	22	17	153	0.65 [0.50, 0.78]	0.87 [0.82, 0.92]
TE	40	11	8	160	0.83 [0.70, 0.93]	0.94 [0.89, 0.97]



Sensitivitet:

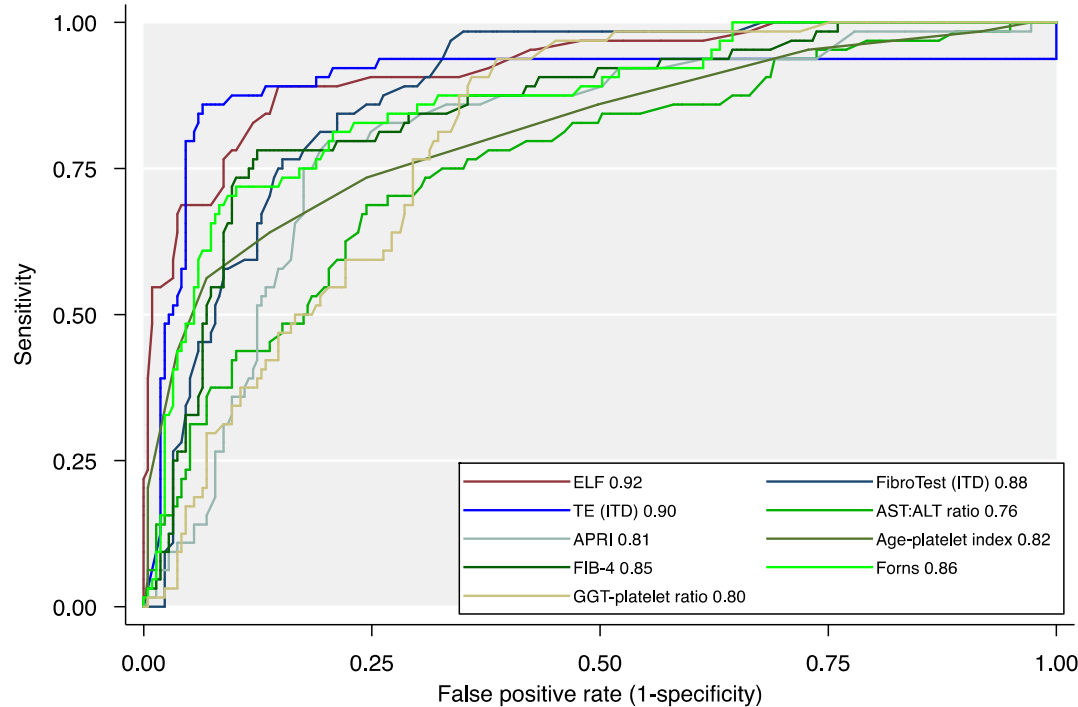
Høj sensitivitet = hvis testen er normal, så er man meget sikker på, at der ikke er begyndende cirrose (rule-out / udelukke sygdom)

Specificitet:

Høj specificitet = hvis testen er abnorm, så er man meget sikker på at der er cirrose (rule-in / diagnosticere sygdom)

Elastografi = leverstivhed

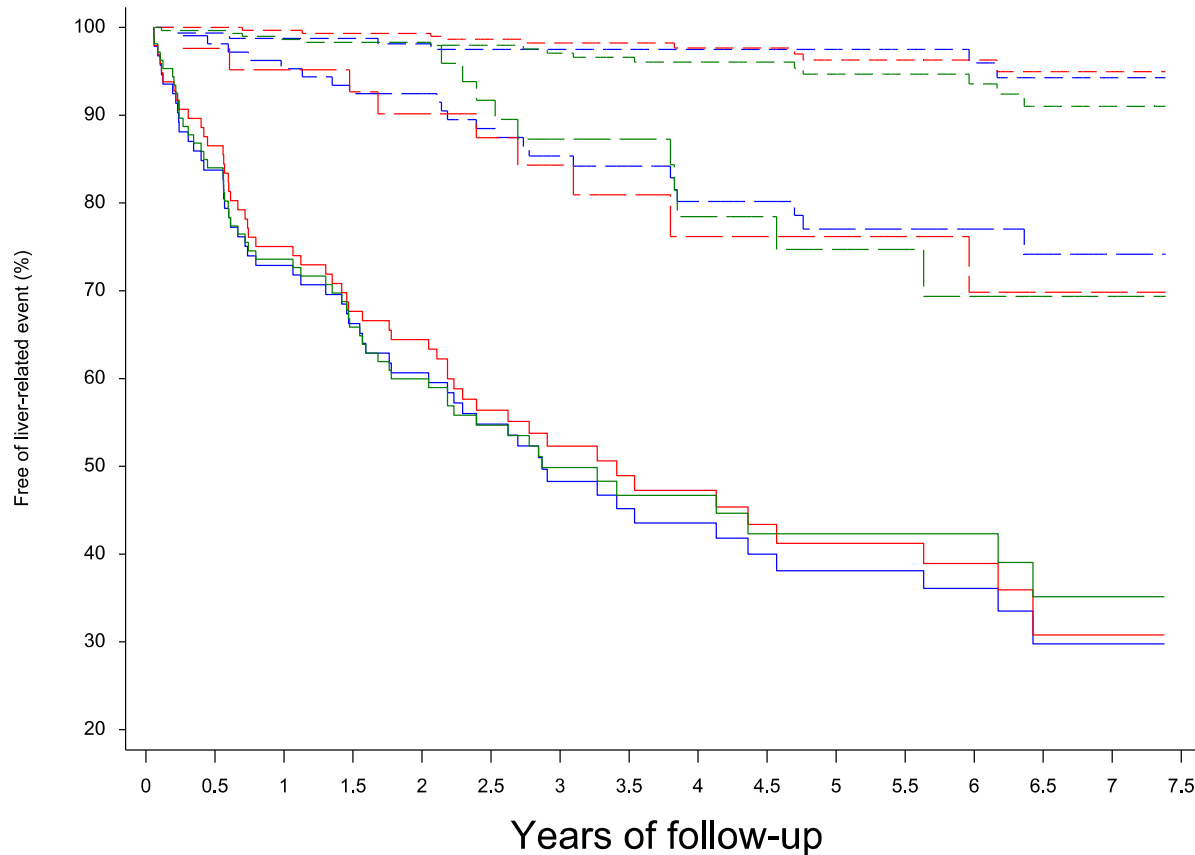
Severe fibrosis ($\geq F3$)



+ metaanalyse med
10 studier og 1026
deltagere.

Nguyen-Khac Lancet Gas Hep
2018

Fibrosetests kan prognosticere



Low risk

- Kleiner F0-1
- TE <10 kPa
- ELF <9.8

Intermediate risk

- Kleiner F2
- TE 10-15 kPa
- ELF 9.8-10.5

High risk

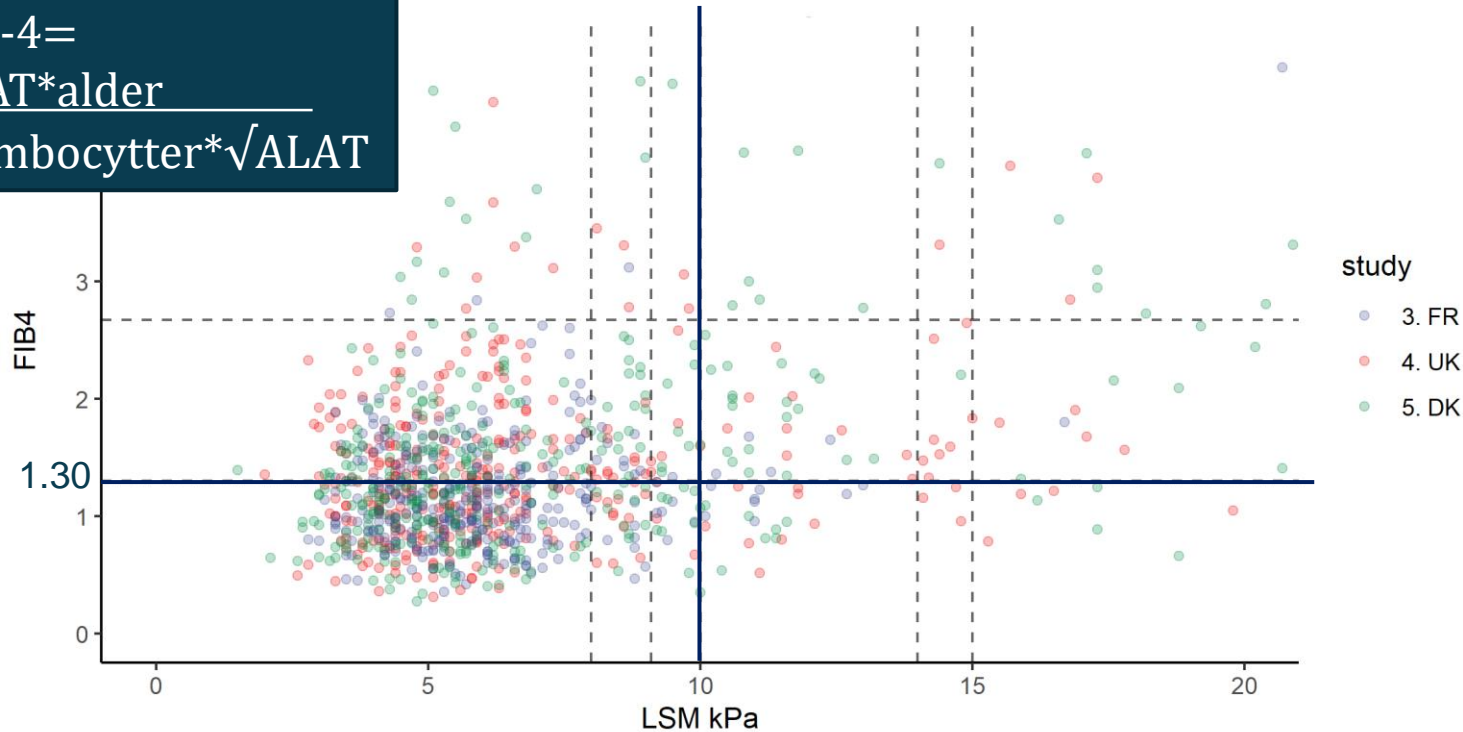
- Kleiner F3-4
- TE >15 kPa
- ELF >10.5

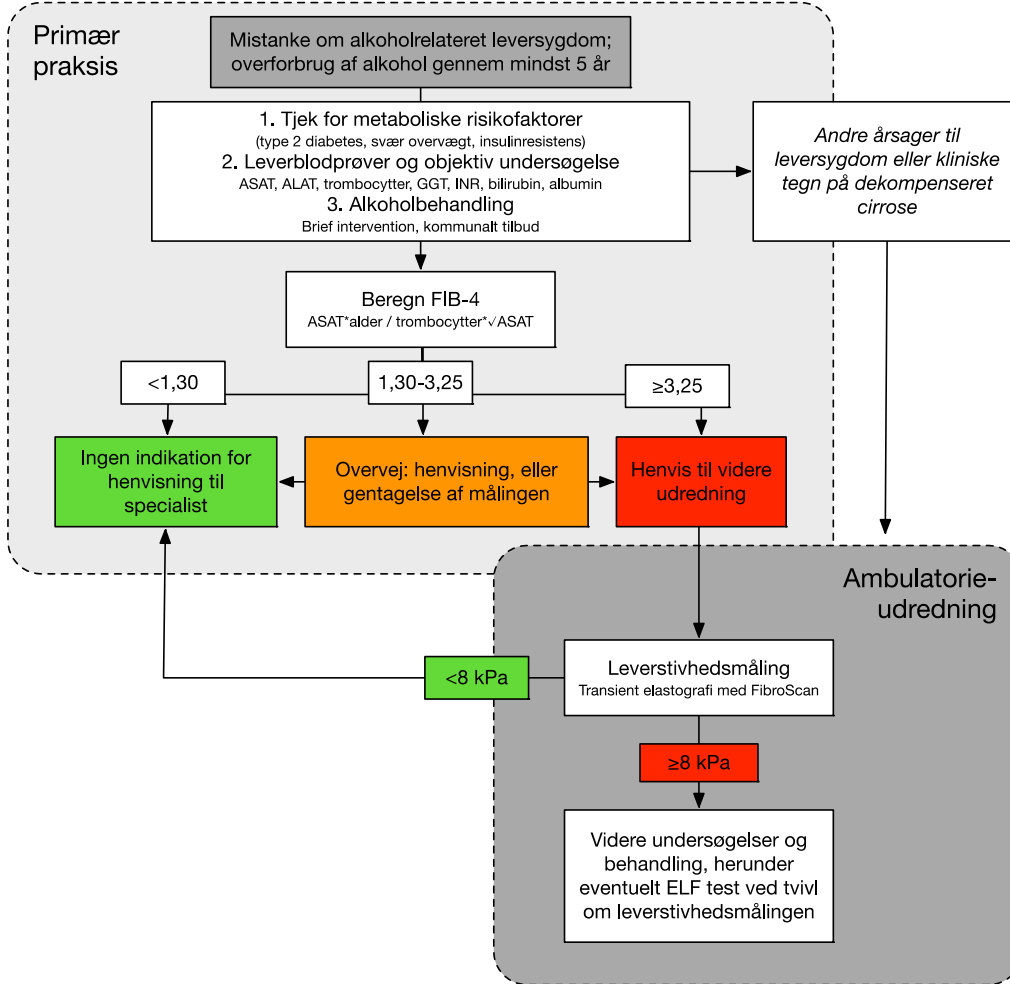
Fibrosetests kan prognosticere

Risk groups	Events/patients in group (%)	Hazard ratio
TE (kPa)		
<10	9/303 (3%)	1
10-15	9/42 (21%)	8.07 (3.20–20.35)
>15	53/98 (54%)	27.94 (13.75–56.78)
ELF		
<9.8	15/300 (5%)	1
9.8-10.5	11/49 (22%)	4.53 (2.08– 9.87)
>10.5	57/108 (53%)	16.94 (9.56–30.04)
FIB-4		
Low*	11/170 (6%)	1
Intermediate*	15/156 (10%)	1.62 (0.74– 3.53)
>2.67	56/103 (54%)	13.39 (7.00–25.64)
Fibrosis stage		
F0-1	6/162 (4%)	1
F2	22/107 (21%)	6.21 (2.52–15.31)
F3-4	55/94 (59%)	26.38 (11.32–61.46)

FIB-4 anbefales ...men den er ikke perfekt...

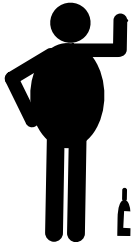
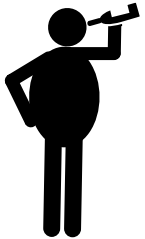
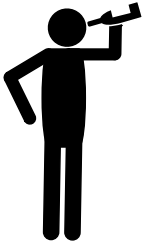
$$\text{FIB-4} = \frac{\text{ASAT} \cdot \text{alder}}{\text{trombocytter} \cdot \sqrt{\text{ALAT}}}$$



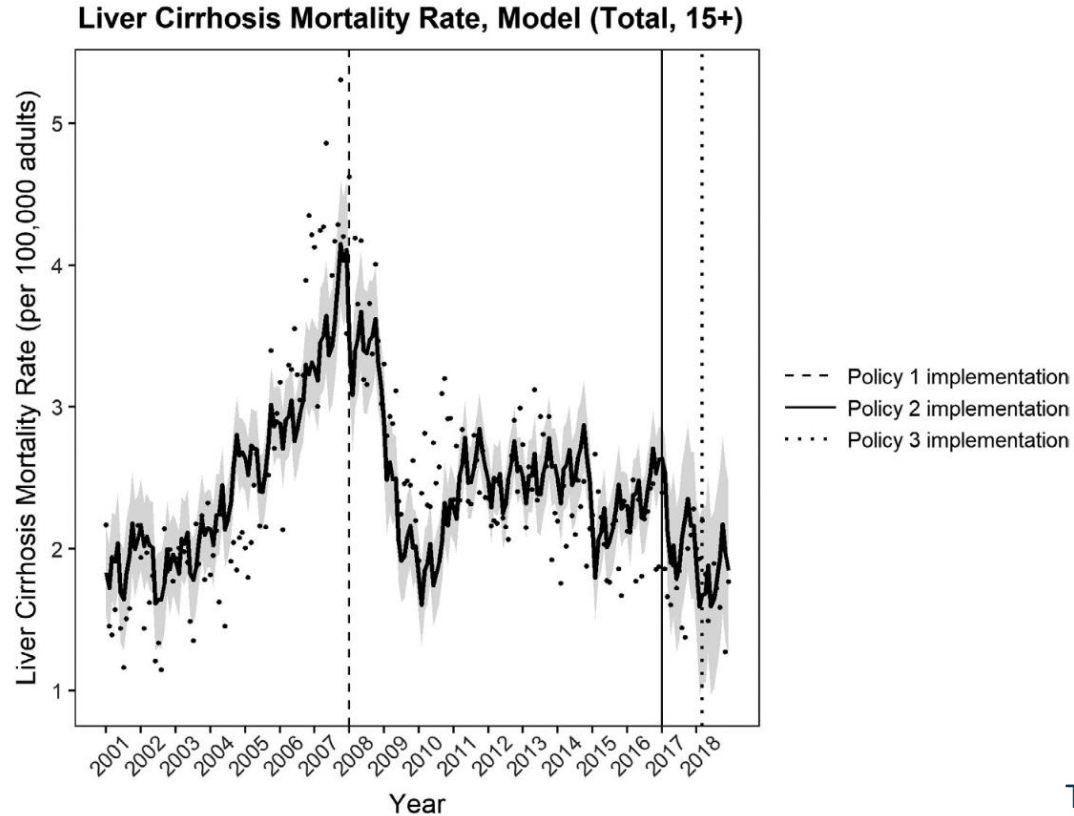


Tag-med-hjem

- Overvej cirrose ved alcohol-overforbrug >15 år. Derudover kan man ikke bruge mængde eller længde til at udlede særlig meget om risiko for cirrose
- Vær særlig opmærksom på patienter med samtidig overvægt eller højt blodsukker/DM2
- Man kan godt have normale levertal (særlig ALAT) og cirrose
- Begynd at bruge FIB-4; hvis ikke ASAT kan bestilles, så se efter trombocytter <150
- Argumentér for en FibroScanner på store alkoholbehandlingcentre?



Det Litauiske eksempel



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